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PLASTER WITH POLYURETHANE FILM AS SUBSTRATE

[PORIURETAN FIRUMU O SHIJITAI TO SURU CHOFUZAI]

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SPECIFICATION

1. Title of the Invention

Plaster with Polyurethane Film as Substrate

2. Scope of Patent Claims

1) A plaster with a polyurethane film as substrate, which is a plaster provided with a drug-containing tacky layer on one side of a polyurethane film substrate and wherein

the substrate is a non-self-adhesive polyurethane film of 60 ~ 110 kg/cm^2 in 100 % modulus and 4 ~ 150 μm in thickness, and

the water vapor transmission of the plaster is 300 ~ 500 g/m^2·24hr.

3. Detailed Description of the Invention

(Field of Industrial Application)

The present invention relates to a plaster with a polyurethane film as substrate.

(Prior Art)

A plaster having a drug-containing tacky layer on one side

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[1]Numbers in the margin indicate pagination in the foreign text.

of a substrate has been utilized for the purpose of obtaining a local or general effect of a drug. As substrates for such a plaster, polyethylene, soft polyvinyl chloride, and so on have been utilized. Such a plaster gives an ODT effect and can effectively absorb a drug because water vapor and the drug are not permeated. However, if a substrate of such materials is used, a skin disorder due to "mune" [transliteration] also easily occurs. Therefore, a plaster with polyurethane, which is a material superior in water vapor transmission, has been suitably used.

Polyurethane film has flexibility, and therefore it has a strong point of being able to easily conform to the skin. Such plasters have been disclosed in Japanese Unexamined Patent 56-22726, Japanese Unexamined Patent 56-32414 and Japanese Unexamined Utility Model 62-148526. However, the polyurethane film generally has flexibility, a so-called weak-kneed (no self-support property), and therefore the film has such a disadvantage that it adheres to an undesirable location or creases without being applied uniformly during application. Therefore, for instance, a tackifier facilitating the application by providing a ground paper sheet on a side opposite to the tacky layer of a substrate has been proposed in the above mentioned Japanese Unexamined Utility Model 62-

148526. However, such a plaster has a disadvantage in that its dose form is complicated.

(Problem to Be Solved by the Invention)

The present invention is to solve the above mentioned previous disadvantage, and its object consists in providing a plaster does not easily cause a skin disorder because it has proper water vapor transmission and can effectively use a drug due to ODT effect. Another object of the present invention consists in providing a plaster that is a plaster having the above mentioned superior properties, that conforms well to the skin because it has flexibility, and that is easily applied because it has some extent of nerve.

(Means for Solving the Problem)

The invented plaster is a plaster provided with a drug-containing tacky layer on one side of a polyurethane film substrate, and the substrate is a non-self-adhesive polyurethane film of 60 ~ 110 kg/cm^2 in 100 % modulus and 4 ~ 150 μm in thickness, and the water vapor transmission of the plaster is 300 ~ 500 $g/m^2 \cdot 24hr$, and thereby the above mentioned objects are achieved.

The polyurethane being a material of substrate used in the invented plaster is obtained by a common reaction of a

diisocyanate and a polyol and, if necessary, a chain extension. As diisocyanates capable of forming a polyurethane, diphenylmethane diisocyanate, dicyclohexylmethane diisocyanate, tolylene diisocyanate, tolidine diisocyanate, hexamethylene diisocyanate, and so on are given. As polyols, polyester polyols such as polyethylene adipate, polybutylene adipate, polycaprolacton, polycarbonate; and polyether polyols such as polyoxytetramethylene glycol are given. As chain extenders, ethylene glycol, butanediol, hexanediol, and so on are given. Polyurethane of 60 ~ 110 kg/cm^2 in 100 % modulus is selected among polyurethanes obtained from the above components. If the 100 % modulus is below 60 kg/cm^2, the film is soft and has no nerve, and the application property of the resulting plaster is bad. If it is above 110 kg/cm^2, the film is hard and has bad conformability in applying it to the skin.

As the adhesives used in the tacky layer of the plaster, alkyl (meth)acrylates (co)polymers; rubber polymers such as styrene-isoprene-styrene block copolymer, styrene-butadiene rubber, polybutene, polyisoprene, butyl rubber, natural rubber, and so on; and silicone polymers are given. As monomers capable of forming the above alkyl (meth)acrylates (co)polymers, alkyl (meth)acrylates and polymeric monomers capable of polymerizing therewith are given. As alkyl (meth)acrylates, (meth)acrylates

having a C_1 ~ C_{18} alkyl group are used, and methyl (meth)acrylate, ethyl (meth)acrylate, butyl (meth)acrylate, 2-ethylhexyl (meth)acrylate, dodecyl (meth)acrylate, and so on are given. As the above mentioned polymeric monomers, (meth)acrylic acid, vinylpyrrolidone, diacetone-acrylamide, (poly)ethylene glycol (meth)acrylate, (poly)propylene glycol (meth)acrylate, 2-hydroxyethyll (meth)acrylate, vinyl acetate, styrene, and so on are given. The alkyl (meth)acrylates are prepared by common processes such as solution polymerization, block polymerization, and so on. If necessary, a tacking agent, liquid rubber, softening agent, and so on are added to the above mentioned rubber adhesives.

Drugs that can be contained in the tacky layer are not specially limited if they are drugs absorbable through the skin. For instance, non-steroid antiinflammatory agents, cortico-steroids, antihistaminic agents, antipruritics, antihyperten-sives, anesthetics, antimycotic agents, antipileptics, coronary vasodilators, hormones, antiphlogistics/analgetics, and local irritants are given.

As non-steroid antiinflammatory agents, pyroxy gum, phenylbutazone, acetyl-salicylic acid, flufenamic acid, mefenamic

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acid, ibuprofen, ketoprofen, flubiprofen, sulindac, indometacine, diclofenac, amfenac, fenbufen, tinoridine, emorfazone, and so on are given.

As corticosteroids, prednisolone, propionic acid, clobetazole, and so on are given. As antihistaminic agents, diphenhydramine, diphenylimidazole, chlorpheniramine, and so on are given. As antipruritics, crotamiton, and so on are given. As antihypertensives, clonidine, nifedipine, propranolol, and so on are given. As anesthetics, lidocaine, benzocaine, and so on are given. As antimycotic agents, clotrimazole, pentamycin, and so on are given. As antipileptics, nitrozebam, meprobamate, and so on are given. As coronary vasodilators, nitroglycerin, isosorbide dinitrate, and so on are given. As hormones, estradiol, and so on are given. As antiphlogistics/analgetics, methyl salicylate, glycol salicylate, glycyrrhizic acid, glycyrrhetic acid, borneol, *Phellodendron amurense* powder, berberine hydrochloridum, and so on are given. As local irritants, capsicum (powder, extract, tincture), capsaicin, vanillylamide pelargonate, terebene oil, di-camphor, benzyl nicotinate, β-butoxyethyl nicotinate, perpermint oil, ℓ-menthol, eucalyptus oil, and so on are given.

The invented plaster is prepared by ordinary methods. For instance, a 40 ~ 150 μm-thick film (substrate) is prepared by

casting or the like with a polyurethane obtained from the above mentioned diisocyanates and polyols. Here, for the polyurethane used and an adhesive base described later, the thickness of the substrate or the tacky layer is determined by selecting their material so that the water vapor transmission of the plaster becomes 300 ~ 500 $g/m^2 \cdot 24hr$. Next, the invented plaster is obtained by preparing a solution or a dispersion containing the above adhesive base, a drug and, if necessary, an absorption assistant, and so on, then coating it on the above substrate and drying. A proper organic solvent or water is used as a solvent for the above solution or dispersion. A method wherein a mixture of above mentioned adhesive base, a drug, and an absorption assistant was heated and melted in place of using a solution or dispersion and then imparted onto a substrate may also be adopted. A method wherein the above mentioned solution, dispersion, or melt is coated on a proper release paper, dried and then a substrate is closely adhered to it is also used. As the above mentioned release paper, a film subjected to a silicon release treatment on one side of polyester, polyethylene-coated wood-free paper, polyolefin-coated glassine paper, polypropylene film or the like is utilized. The release paper is used for the purpose of protecting the tacky layer. The thickness of the tacky layer formed above is usually within the range of about 30

μm ~ 2 mm, and a drug is uniformly dispersed therein. As is described above, the water vapor transmission of the resulting adhesive is 300 ~ 500 g/m^2·24hr. This value is a value measured by a test method for adhesive tape and adhesive sheet of JIS Z 0237. If the above mentioned water vapor transmission is below 300 g/m^2·24hr, contact dermatitis or redness of the skin caused by "mune" [transliteration] easily occurs when the plaster is pasted to the surface of the skin. If it is above 500 g/m^2·24hr, the absorptivity of the drug is lowered.

(Operation)

Thus, the absorptivity of drug of the plaster is good, and it is difficult for a skin disorder to occur because a polyurethane film having a specific water vapor transmission is utilized as a substrate in the present invention. The substrate is also superior in its application property of the plaster because it has a specific thickness and a modulus. A ground paper (process paper) for keeping the substrate in a prescribed shape at the time of application is not needed. The plaster also has no feeling of physical disorder at the time of application. Such a plaster is suitably used in the treatment or prevention of various diseases by containing various drugs according to the purposes.

(Embodiment examples)

The present invention is described by embodiment examples below.

Embodiment example 1

1 g of difenhydramine was added to 200 g of an acrylic emulsion adhesive [a copolymer of methacrylic acid and 2-ethylhexyl acrylate (3:97); solid content 50 %] and then uniformly dispersed. This formulated solution was extended on a polyethylene-coated glassine paper, dried at 60° C and then transferred

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to a polyurethane film A (thickness: 70 μm, 100 % modulus: 80 kg/cm^2) to obtain a plaster. When the water vapor transmission of this plaster was measured by a test method for adhesive tape and adhesive sheet of JIS Z 0237, it was 400 g/m^2·24hr. 2 × 2 cm of the resulting plaster was applied to the upper arm of a panel, the application property (ease of application) and the application feeling after it is applied were examined. The results are shown together with comparative examples 1 ~ 3 described later. In the item of application property of Table 1, O indicates that the plaster has a proper nerve and can be uniformly applied in application. Δ indicates that the plaster is soft and has no nerve, creases, or is hard to be uniformly

applied. In the item of application feeling, ○ indicates that the plaster becomes conformable for the surface of skin and a feeling of physical disorder is not sensed, and Δ indicates that a feeling of physical disorder (stiffness of the skin, and so on) is slightly sensed in flexing parts such as joints.

Comparative example 1

It was the same as embodiment example 1 except that a soft polyvinyl chloride film of 173 kg/cm^2 in 100 % modulus was used as a substrate.

Comparative example 2

It was the same as embodiment example 1 except that a polyurethane film B of 50 kg/cm^2 in 100 % modulus and 34 μm in thickness was used as a substrate.

Comparative example 3

It was the same as embodiment example 1 except that a polyethylene film of 130 kg/cm^2 in 100 % modulus and 50 μm in thickness was used as a substrate.

Table 1

	支持体			貼付薬特性	
	組成	100%モジュラス (kg/cm²)	厚み (μm)	貼付感	貼付後 (経時変化)
実施例1	ポリウレタンA	50	75	○	○
比較例1	塩化ビニル 塩化ビニル	173	75	△	○
比較例2	ポリウレタンB	50	34	○	△
比較例3	ポリエチレン	139	50	△	○

	A			B	
	C	D	E	F	G
H	L				
I	M				
J	N				
K	O				

Translator's note:

A Substrate

B Property of plaster

C Composition

D 100 % modulus (kg/cm^2)

E Thickness (μm)

F Application feeling

G Applicability (ease of application)

H Embodiment example 1

I Comparative example 1

J Comparative example 2

K Comparative example 3

L Polyurethane A

M Soft polyvinyl chloride

N Polyurethane B

O Polyethylene

From Table 1, it is known that the invented plaster is superior in applicability and application feeling. By contrast, the plaster having a substrate of below 60 kg/cm^2 in 100 %

modulus (comparative example 2) has bad applicability because the substrate is soft and has no nerve. Conversely, the plasters having a substrate of the above mentioned 110 kg/cm^2 in 100 % modulus (comparative example 1 and 3) have bad conformability to the skin and an inferior application feeling.

Embodiment example 2

78.12 g of an acrylic adhesive [a copolymer of methacrylic acid and 2-ethylhexyl acrylate (3:97)], 6.25 g of indometacine, 3.91 g of soybean lecithin, and 11.72 g of isopropyl myristate were homogeneously dissolved in 200 g of ethyl acetate. A plaster was similarly prepared with this formulated solution as in embodiment example 1. The water vapor transmission of the resulting tape was tested according to a test method for adhesive tape and adhesive sheet of JIS Z 0237 (JIS Z 0237). Next, the plaster was cut to test pieces of about 20 mm in diameter, pasted in a flexing part of the upper arm of a panel for 24 hr, and the extent of irritation of the skin was tested with the test pieces. A drug test using the skin of nude mice was carried out by the following method. Respective results are shown in Table 2.

<Permeability of drug for skin of nude mice>

Skin extracted from the back of nude mice is set in a Franz type diffusion cell, and the plaster is pasted to this skin. A

phosphoric acid buffer solution (pH 7.2) is used as a receptor solution. The quantity of indometacine migrated from the plaster to the receptor solution through the skin is measured by HPLC, and the transmissivity of indometacine to the skin is calculated by the following expression.

$$\text{Transmissivity to skin (\%)} = \frac{\text{Content of drug in receptor solution after 24 hr}}{\text{Content of drug in plaster}} \times 100$$

Comparative example 4

It was the same as embodiment example 2 except that a soft polyvinyl chloride film of 173 kg/cm^2 in 100 % modulus was used as a substrate.

Comparative example 5

It was the same as embodiment example 2 except that a polyurethane film B of 50 kg/cm^2 in 100 % modulus and 34 μm in thickness was used as a substrate.

Comparative example 6

It was the same as embodiment example 2 except that a laminate film (a laminate of polyethylene terephthalate and

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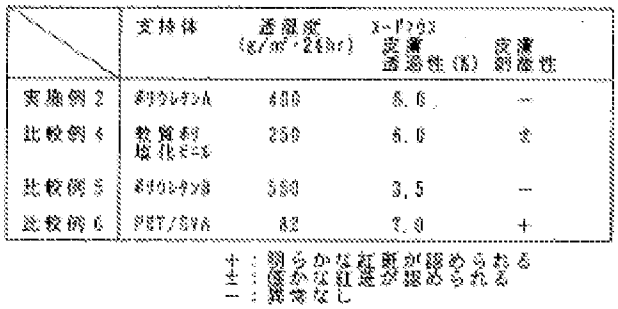
ethylene-vinyl acetate copolymer) of 31 μm in thickness was used as a substrate.

Table 2



	A	B	C	D
E	I			
F	J			
G	K			
H	L			

+: Clear erythema is found

±: Slight erythema is found

-: no abnormality

Translator's note:

A Substrate

B water vapor transmission (g/m^2≅24 hr)

C Transmissivity to skin of nude mice (%)

D Irritation to skin

E Embodiment example 2

F Comparative example 4

G Comparative example 5

H Comparative example 6

I Polyurethane A

J Soft polyvinyl chloride

K Polyurethane B

L PET/EVA

From Table 2, the invented plaster has good water vapor transmission and therefore does not cause erythema, even if it is pasted for a long period of time. It also has good skin permeability for the drug. By contrast, a plaster with low water vapor transmission has good permeability for the drug, but erythema due to irritation of the skin is found. A plaster with high water vapor transmission does not cause irritation of the skin but has low permeability for the drug.

(Effects of the Invention)

Thus, according to the present invention, a drug-containing plaster absorbing a drug effectively, having excellent applicability and good conformability for the skin without causing a skin disorder is obtained. Such a plaster is suitably used in the treatment and prevention of various diseases by containing various drugs.